UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,333	09/08/2006	Tatsuo Hoshino	4662-217	6631

23117 7590 02/26/2008

NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
MACAULEY, SHERIDAN R	
ART UNIT	PAPER NUMBER
1651	

MAIL DATE	DELIVERY MODE
02/26/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,333	HOSHINO ET AL.	
	Examiner	Art Unit	
	Sheridan R. MacAuley	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/26/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-10 are pending and examined on the merits in this office action.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1-3, 5, 7 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Yin et al. (US 4,935,359) when taken in view of Sugisawa et al. (Biosci. Biotechnol. Biochem., 2005, 69:659-662). Claim 1 recites a process for the production of vitamin C comprising converting a substrate into vitamin C in a medium using a microorganism belonging to the genus *Ketogulonicigenium*. Claim 2 recites the process of claim 1 wherein the substrate is selected from the group consisting of D-sorbitol, L-sorbose, L-sorbosone, L-gulose and L-gulono-gamma-lactone. Claim 3 recites the process according to claim 1 for the production of vitamin C comprising contacting the microorganism with the substrate in a reaction mixture and purifying vitamin C from the reaction mixture. Claim 5 recites the process of claim 1 wherein the microorganism is selected from the group consisting of *Ketogulonicigenium robustum*, *Ketogulonicigenium vulgare*, or mutants thereof. Claims 7 and 8 recite the process of claims 1 or 7 wherein the process is carried out at a pH of about 4.0 to about 9.0 and a

temperature of about 13 to about 36 degrees C, or at a pH of about 5.0 to about 8.0 at a temperature of about 18 to about 33 degrees C, respectively.

3. Yin teaches a process for the production of vitamin C via 2-keto-L-gulonic acid by contacting L-sorbose with the microorganism *Gluconobacter oxydans* DSM 4025 to produce 2-keto-L-gulonic (col. 5, line 54-col. 6, line 8). Sugisawa teaches that *Gluconobacter oxydans* DSM 4025 is synonymous with *Ketogulonicigenium vulgare* DSM 4025 (p. 659, par. 1); thus, Yin uses the microorganism recited by the claims. Yin teaches that the reaction is carried out at a pH of 5 to 8 and a temperature of about 25 to about 35 degrees C (col. 6, lines 30-32). Yin teaches that the 2-keto-L-gulonic acid may optionally be converted to vitamin C (i.e. L-ascorbic acid) while in the reaction mixture, and the vitamin C can then be purified therefrom (col. 3, lines 53-65). Sugisawa also teaches that the organism produces vitamin C from L-sorbose directly under the conditions taught by Yin (p. 659, par. 2, 3, p. 660, par. 1-3). Thus, vitamin C is inherently produced in the process of Yin even when the optional step of converting 2-keto-L-gulonic acid to vitamin C is not performed.

4. Therefore, Yin anticipates all of the limitations of the cited claims.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-3 and 5-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yin et al. (US 4,935,359) in view of Stoddard et al. (US 6,316,231) when taken in view of Sugisawa et al. (Biosci. Biotechnol. Biochem., 2005, 69:659-662), Urbance et al. (International Journal of Systematic and Evolutionary Microbiology, 2001, 51:1059-1070; cited in IDS), and NCBI (Taxonomy browser (*Ketogulonicigenium vulgare*)). Claim 1 recites a process for the production of vitamin C comprising converting a substrate into vitamin C in a medium using a microorganism belonging to the genus *Ketogulonicigenium*. Claim 2 recites the process of claim 1 wherein the substrate is

selected from the group consisting of D-sorbitol, L-sorbose, L-sorbosone, L-gulose and L-gulono-gamma-lactone. Claim 3 recites the process according to claim 1 for the production of vitamin C comprising contacting the microorganism with the substrate in a reaction mixture and purifying vitamin C from the reaction mixture. Claims 5 and 6 recite the process of claim 1 wherein the microorganism is selected from the group consisting of *Ketogulonicigenium robustum*, *Ketogulonicigenium vulgare*, or mutants thereof, specifically *K. robustum* NRRL B-21627, *K. vulgare* NRRL B-30035, *K. vulgare* NRRL B-30036, or *K. vulgare* NRRL B-30037. Claims 7 and 8 recite the process of claims 1 or 7 wherein the process is carried out at a pH of about 4.0 to about 9.0 and a temperature of about 13 to about 36 degrees C, or at a pH of about 5.0 to about 8.0 at a temperature of about 18 to about 33 degrees C, respectively.

9. Yin teaches a process for the production of vitamin C via 2-keto-L-gulonic acid by contacting L-sorbose with the microorganism *Gluconobacter oxydans* DSM 4025 to produce 2-keto-L-gulonic (col. 5, line 54-col. 6, line 8). Yin teaches that the reaction is carried out at a pH of 5 to 8 and a temperature of about 25 to about 35 degrees C (col. 6, lines 30-32). Yin teaches that the 2-keto-L-gulonic acid may be converted to vitamin C (i.e. L-ascorbic acid) while in the reaction mixture, and the vitamin C can then be purified therefrom (col. 3, lines 53-65). Sugisawa teaches that *Gluconobacter oxydans* DSM 4025 was renamed to *Ketogulonicigenium vulgare* DSM 4025 (p. 659, par. 1); thus, Yin uses the microorganism recited by the claims. Sugisawa also teaches that the organism produces vitamin C from L-sorbose directly under the conditions taught by Yin (p. 659, par. 2, 3, p. 660, par. 1-3). Thus, vitamin C is inherently produced in the

process of Yin even when the optional step of converting 2-keto-L-gulonic acid to vitamin C is not performed. Yin does not teach the use of one of the claimed bacterial strains in the process.

10. Stoddard teaches a process for the production of 2-keto-L-gulonic acid by contacting L-sorbose with the bacterial strain NRRL-21627 or mutants and variants thereof (col. 2, lines 25-36). Urbance teaches that bacterial strain NRRL-21627 was renamed to *Ketogulonigenium robustum* NRL-21627 (abstract), and NCBI teaches that *Ketogulonigenium robustum* is synonymous with *Ketogulonicigenium robustum*; thus, Stoddard teaches the use of one of the claimed microbial strains.

11. At the time of the invention, a process for the production of vitamin C comprising nearly all of the claimed elements was known, as taught by Yin. It was further known that 2-keto-L-gulonic acid could be produced from L-sorbose by *K. robustum* NRRL B-21627, as taught by Stoddard. One of ordinary skill in the art would have been motivated to use the bacterial strain taught by Stoddard in the method of Yin because Stoddard teaches that NRRL B-21627 produces higher yields of 2-keto-L-gulonic acid than the *Ketogulonicigenium vulgare* strain taught by Yin (col. 10-11, example 3, col. 11, table 6). One of ordinary skill in the art would have had a reasonable expectation of success in combining these references because both bacterial strains were known at the time of the invention to be useful for the production of 2-keto-L-gulonic acid under similar conditions. It would therefore have been obvious to one of ordinary skill in the art to combine the teachings discussed above to arrive at the claimed invention.

12. Claims 1-10 rejected under 35 U.S.C. 103(a) as being unpatentable over Yin et al. (US 4,935,359) in view of Stoddard et al. (US 6,316,231) when taken in view of Sugisawa et al. (Biosci. Biotechnol. Biochem., 2005, 69:659-662), Urbance et al. (International Journal of Systematic and Evolutionary Microbiology, 2001, 51:1059-1070; cited in IDS), and NCBI (Taxonomy browser (*Ketogulonicigenium vulgare*)) as applied to claims 1-3 and 5-8 above, and further in view of Asakura et al. (Biosci. Biotechnol. Biochem. 1999, 63:46-53).

13. Claim 1 recites a process for the production of vitamin C comprising converting a substrate into vitamin C in a medium using a microorganism belonging to the genus *Ketogulonicigenium*. Claim 2 recites the process of claim 1 wherein the substrate is selected from the group consisting of D-sorbitol, L-sorbose, L-sorbosone, L-gulose and L-gulono-gamma-lactone. Claim 3 recites the process according to claim 1 for the production of vitamin C comprising contacting the microorganism with the substrate in a reaction mixture and purifying vitamin C from the reaction mixture. Claim 4 recites the process according to claim 1 for the production of vitamin C comprising contacting the microorganism with the L-sorbosone in a reaction mixture and purifying vitamin C from the reaction mixture. Claims 5 and 6 recite the process of claim 1 wherein the microorganism is selected from the group consisting of *Ketogulonicigenium robustum*, *Ketogulonicigenium vulgare*, or mutants thereof, specifically *K. robustum* NRRL B-21627, *K. vulgare* NRRL B-30035, *K. vulgare* NRRL B-30036, or *K. vulgare* NRRL B-30037. Claims 7 and 8 recite the process of claims 1 or 7 wherein the process is carried out at a pH of about 4.0 to about 9.0 and a temperature of about 13 to about 36

degrees C, or at a pH of about 5.0 to about 8.0 at a temperature of about 18 to about 33 degrees C, respectively. Claims 9 and 10 recite the process according to claim 1 wherein the process is carried out at an L-sorbosone concentration of about 2 to about 120 mg/l, particularly about 4 to about 100 mg/l.

14. Yin teaches a process for the production of vitamin C via 2-keto-L-gulonic acid by contacting L-sorbose with the microorganism *Gluconobacter oxydans* DSM 4025 to produce 2-keto-L-gulonic (col. 5, line 54-col. 6, line 8). Yin teaches that the reaction is carried out at a pH of 5 to 8 and a temperature of about 25 to about 35 degrees C (col. 6, lines 30-32). Yin teaches that the 2-keto-L-gulonic acid may be converted to vitamin C (i.e. L-ascorbic acid) while in the reaction mixture, and the vitamin C can then be purified therefrom (col. 3, lines 53-65). Sugisawa teaches that *Gluconobacter oxydans* DSM 4025 was renamed to *Ketogulonicigenium vulgare* DSM 4025 (p. 659, par. 1); thus, Yin uses the microorganism recited by the claims. Yin does not teach the use of one of the claimed bacterial strains in the process.

15. Stoddard teaches a process for the production of 2-keto-L-gulonic acid by contacting L-sorbose with the bacterial strain NRRL-21627 or mutants and variants thereof (col. 2, lines 25-36). Urbance teaches that bacterial strain NRRL-21627 was renamed to *Ketogulonigenium robustum* NRL-21627 (abstract), and NCBI teaches that *Ketogulonigenium robustum* is synonymous with *Ketogulonicigenium robustum*; thus, Stoddard teaches the use of one of the claimed microbial strains.

16. As discussed above, it would have been obvious at the time of the invention to combine the teachings of Yin and Stoddard to arrive at nearly all of the elements of the

claimed invention. Neither of the references, however, teaches the production of vitamin C from L-sorbosone.

17. Asakura teaches a method for the production of 2-keto-L-gulonic acid from strain DSM 4025 (abstract). Asakura teaches that the enzyme involved in the production of 2-keto-L-gulonic acid converts both L-sorbose and L-sorbosone into 2-keto-L-gulonic acid (abstract).

18. At the time of the invention, it would have been obvious to develop a method for the production of vitamin C comprising nearly all of the claimed elements, as taught by Yi and Stoddard. Further, a method for the production of 2-keto-L-gulonic acid from L-sorbosone using strain DSM 4025 was known, as taught by Asakura. One of ordinary skill in the art would have been motivated to combine these teachings because the activity of the enzyme was shown to be higher or L-sorbosone than on L-sorbose (p. 50, table 2); one would thus have recognized that L-sorbosone could replace L-sorbose in the method. Furthermore, both Yin and Stoddard discuss the use of the substrate at the claimed concentration (Stoddard uses 50-200 mg/ml (5-20%; col. 5, lines 36-38) and Yin uses 80 or 120 mg/ml (8 or 12%; col. 5, examples 1 and 2). One of ordinary skill in the art would therefore have been motivated to use L-sorbosone in the claimed concentration in the combined method. One of ordinary skill in the art would have had a reasonable expectation of success in combining these teachings because it was known in the art at the time of the invention that the same microorganism was capable of producing 2-keto-L-gulonic acid from both L-sorbosone and L-sorbose, and methods for cultivating the organism under conditions for the production of 2-keto-L-gulonic acid

were also known. It would therefore have been obvious to one of ordinary skill in the art to combine the teachings discussed above to arrive at the claimed invention.

19. Thus, the claimed invention as a whole was *prima facie* obvious over the combined teachings of the prior art.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan R. MacAuley whose telephone number is (571)270-3056. The examiner can normally be reached on Mon-Thurs, 7:30AM-5:00PM EST, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SRM
/Ruth A. Davis/
Primary Examiner, Art Unit 1651